CLAIMS

What is claimed:

1. A method of treating a subject suffering from a metabolic disorder comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, such that the metabolic disorder is treated.

2. A method of treating a subject suffering from a metabolic disorder comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that the metabolic disorder is treated.

3. A method of treating a subject suffering from a metabolic disorder comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR)

comprising the amino acid sequence of SEQ ID NO: 2, such that the metabolic disorder is treated.

4. The method of any one of claims 1, 2, and 3, wherein the antibody, or antigen-binding fragment thereof, is D2E7.

5. The method of any one of claims 1, 2, and 3, wherein the metabolic disorder is diabetes or obesity.

6. The method of claim 5, wherein the diabetic disorder is selected from the group consisting of type 1 diabetes mellitus, type 2 diabetes mellitus, diabetic retinopathy, diabetic ulcerations, neuropathy, retinopathy ulcerations, peripheral neuropathy, diabetic macrovasculopathy.

7. A method of treating a subject suffering from diabetes or obesity comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, such that said diabetes or obesity is treated.

8. A method of treating a subject suffering from diabetes or obesity comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that said diabetes or obesity is treated.

9. A method of treating a subject suffering from diabetes or obesity comprising administering a therapeutically effective amount a TNFα antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that said diabetes or obesity is treated.

10. The method of any one of claims 7, 8, or 9, wherein the TNFα antibody, or antigen binding fragment thereof, is D2E7.

11. The method of any one of claims 7, 8, or 9, wherein the diabetic disorder is selected from the group consisting of type 1 diabetes mellitus, type 2 diabetes mellitus, diabetic retinopathy, diabetic ulcerations, neuropathy, retinopathy ulcerations, peripheral neuropathy, diabetic macrovasculopathy.

12. The method of any one of claims 7, 8, or 9, wherein the TNFα antibody is administered with at least one additional therapeutic agent.

13. A method for inhibiting human TNFα activity in a human subject suffering from a metabolic disorder comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

14. The method of claim 13, wherein the metabolic disorder is diabetes or obesity.

15. The method of claim 14, wherein the diabetic disorder is selected from the group consisting of type 1 diabetes mellitus, type 2 diabetes mellitus, diabetic retinopathy, diabetic ulcerations, neuropathy, retinopathy ulcerations, peripheral neuropathy, diabetic macrovasculopathy.

16. The method of any one of claims 13, 14, and 15, wherein the TNFα antibody, or antigen-binding fragment thereof, is D2E7.

17. A method for inhibiting human TNFα activity in a human subject suffering from diabetes or obesity, comprising administering a therapeutically effective amount of a TNFα antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

18. The method of claim 17, wherein the diabetic disorder is selected from the group consisting of type 1 diabetes mellitus, type 2 diabetes mellitus, diabetic retinopathy, diabetic ulcerations, neuropathy, retinopathy ulcerations, peripheral neuropathy, diabetic macrovasculopathy.

19. The method of claim 17 or 18, wherein the antibody, or antigen binding fragment thereof, is D2E7.

20. A method of treating a subject suffering from a metabolic disorder comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the metabolic disorder is treated.

21. The method of claim 18, wherein the metabolic disorder is diabetes or obesity.

22. The method of claim 21, wherein the diabetic disorder is selected from the group consisting of type 1 diabetes mellitus, type 2 diabetes mellitus, diabetic retinopathy, diabetic ulcerations, neuropathy, retinopathy ulcerations, peripheral neuropathy, diabetic macrovasculopathy.

23. A method of treating a subject suffering from diabetes or obesity comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that said diabetes or obesity is treated.

24. A method of treating a subject suffering from a metabolic disorder comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, and at least one additional therapeutic agent to the subject, such that the metabolic disorder is treated.

25. A kit comprising:

a) a pharmaceutical composition comprising a TNFα antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier; and

b) instructions for administering to a subject the TNFα antibody pharmaceutical composition for treating a subject who is suffering from a metabolic disorder.

26. A kit according to claim 23, wherein the TNFα antibody, or an antigen binding portion thereof, is D2E7.